DOCKET NO.: RTS-0678US **PATENT**

REMARKS

The status of the claims is as follows. Claims 1, 3-9, 11-18, 22-40, 44 and 49-60 are pending. Claims 18, 23-40 and 49-57 are withdrawn. Claim 1 is amended herein.

Claim 1 as amended finds support for example on page 23, lines 9 to 14 which states "[t]he oligomeric compounds are also targeted to ... regions of the target nucleobase sequence ...comprising nucleobases ...901-950. Claim 1 also finds support on page 77, Table 1 which discloses SEQ ID NOs 35-38 including their sequence and target site. Claim 1 also finds support, for example, on page 22, lines 2-5 and page 23, line 29 which indicates that the compound can have an 8-nucleobase portion of an active antisense compound targeted to a specific active region.

Elections/Restrictions

Applicant submits that withdrawn claims 18, 33-40, and 49-57 are related to the claims being prosecuted herein as product and process of use claims and are subject to rejoinder upon allowance of a linking product claim. See e.g., p.7 of the Office Action mailed May 27, 2005.

Rejection under 35 USC § 112 – Written Description

Claims 1, 3-9, 11, 12, 14-17, 22, 44, 58 and 59 are rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement because 1) the claims allegedly encompass a genus of molecules which are different than those explicitly disclosed in the specification and 2) due to the genus encompassing numerous alternatives, there is allegedly an absence of sufficient recitation of distinguishing identify characteristics. Applicant respectfully disagrees. Claim 1 is amended herein, therefore, the following remarks concern the claims as amended.

The instant specification provides a target mRNA sequence for diacylglycerol acyltransferase 2 (See e.g., SEQ ID NO 4). The specification states that the invention includes antisense compounds that inhibit the production of diacylglycerol acyltransferase 2. The specification describes art recognized methods for making and screening compounds that are complementary to the target sequence (See e.g., Examples 2-10).

As provided in the PTO Written Description Guidelines with regard to antisense compounds (see e.g., http://www.uspto.gov/web/menu/written.pdf), the general knowledge in the art is that any full-length complement of a target mRNA inhibits the function of the mRNA. Thus, one of skill in the art would view applicant's disclosure of a coding sequence, with the statement that the invention includes antisense oligonucleotides, as an implicit disclosure that the full-length complement of target is an antisense oligonucleotide. Further, it is generally accepted in the art that oligonucleotides complementary to an mRNA, including a full length complement or fragment thereof, have antisense activity when they match accessible regions on the target mRNA. Generally, the closer the complementary fragment is to full length, the greater the likelihood it will have antisense activity. Additionally, the procedures for making oligonucleotide fragments of the target complement are conventional, e.g., and specified fragment can be ordered from a commercial synthesizing service. The procedures for screening for antisense activity are also conventional, and the specification describes the assays to be conducted. The experience accumulated in the art with gene walking is that numerous regions of a target are accessible, that these regions are identified routinely, and that antisense oligonucleotides are complementary to these accessible regions. Longer length complements match multiple accessible regions and shorter fragments match fewer accessible regions. As a result, in considering the specification's disclosure, the target sequence provided defines and limits the structure of any effective antisense molecules such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claims.

Further, the specification provides specific examples of accessible regions including the region of claim 1 as well as specific compounds targeted to the regions, namely SEQ ID NOs 35-38. SEQ ID NOs 35-38 specifically fall within the region of claims 1. The sequences are overlapping and complementary over 34 nucleotides of the claimed range. Further, it is understood in the art that the sequence of an antisense compound need not be 100% complementary to that of its target nucleic acid (See page 12, lines 8-10 of the instant specification). Also, as disclosed, the oligonucleotides of the present invention include variants in which a different base is present at one or more of the nucleotide positions in the oligonucleotide. For example, if the first nucleotide is an adenosine, variants may be produced which contain thymidine, guanosine or cytidine at this position. This may be done at any of the positions of the oligonucleotide. These oligonucleotides are then tested using

the methods described herein to determine their ability to inhibit expression of diacylglycerol acyltransferase 2 mRNA. (See page 15, lines 10-19). It readily understood by those of skill in the art that such variants can be made and need not be completely complementary to the target.

Considering the specification's disclosure of 1) the target sequence with defines and limits the structure of any effective antisense compounds such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim, and 2) the functional characteristics of the claimed invention as well as a routine art-recognized method of screening for compounds with provide further distinguishing characteristics fo the claimed inventions, along with 3) the general level of knowledge and skill in the art, one skilled in the art would conclude that applicant was in possession of the invention.

Fees

It is believed that no fee is due with this response. The director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or during the pendency of this application, or credit any overpayment in any fees to our Deposit Account Number 50-0252.

Conclusion

In view of the above, applicant respectfully requests prompt and favorable action on all pending claims. In the event that any matters remain to be resolved, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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